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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,130	05/14/2001	Keith H.S. Campbell	105434.105001	8898

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,130	CAMPBELL, KEITH H.S.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 2, 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-88* is/are pending in the application.

4a) Of the above claim(s) *51-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-50 and 56-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a national stage filing of PCT/GB00/00086, filed January 13, 2000 (amended July 12, 2000 and October 13, 2000), which claims benefit to provisional application 60/130,546 filed April 22, 1999 and claims benefit to foreign application 9900734.6 filed January 13, 1999 in Great Britain.

Applicants amendment filed August 25, 2003 has been received and entered. Claims 1-41 have been canceled. Claims 42-44, 56, 67 have been amended. Claims 83-88 have been added. Claims 42-88 are pending and currently under examination.

Election/Restriction

Applicant's election without traverse of Group I, claims 42-50 and 56-82, is acknowledged. Newly added claims 83-88 are dependent on claims encompassing the elected invention, therefore will be examined with the instantly elected invention. Claims 51-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse.

In addition, Applicant has elected the pig as the species of animal. Upon review of the claimed invention and the art of record, the election of species is withdrawn because it would not constitute an undue burden to examine all the species specifically recited in the claims.

Applicant notes the differences between the claimed invention and that disclosed by Strelchenko *et al.* used in the basis for the restriction requirement. In the restriction requirement

it was indicated that the method of producing a reconstituted embryo by passing the nuclear donor through more than one recipient oocyte has been previously disclosed in the art. Strelchenko *et al.* (WO 98/39416) describes the production of multiple nuclear transfer units and methods of culturing in order to produce a cloned animal (see for example schemes in figures 3 and 4 and page 55 Section III). Strelchenko *et al.* teach a method of generating a cloned mammal be serially passaging by nuclear transfer into an oocyte using nuclear transfer technology. It is noted that claim 42 has been amended to differentiate the claimed invention from that specifically disclosed by Strelchenko *et al.*, however this does not obviate the anticipation of Strelchenko *et al.* over the original claims that broadly encompassed the methods of Strelchenko *et al.* wherein the serial transplantation could be accomplished after culturing the resulting oocyte as taught by Strelchenko *et al.* The present claims as amended exclude this culture step. Subsequently, the embryo/fetus can be used to generate a cloned mammal. Because the method encompassed by claim 42 for providing an embryo has been previously disclosed in the art, there is not special technical feature which links the various methods instantly claimed.

Claims 42-50 and 56-88 are under examination to the extent they encompass the elected invention of a method of producing an animal embryo comprising passing a diploid nuclear donor through a first recipient oocyte, then into a second oocyte or zygote, the embryo produced by this method, a cell line produced from the embryo and a method of producing an animal from said embryo.

Claim Objections

Claim 42 is objected to because of the following informalities: the elected invention is drawn to using a diploid cell in the nuclear transfer protocols, however the pending claim still encompasses the use of a cell with any ploidy. The claims should be amended to encompass the elected invention of using of using a diploid cell.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 77-79 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The basis of this rejection focuses on the fact that the claims are drawn to a product by process, however the resulting animal is simply an animal with no definable characteristics that would distinguish it from any other animal that exists in nature. With respect to the embryo, the claim reads on an embryo in any context including *in utero*. The rejection of claim 77 can be overcome by amending the claims to encompass an isolated embryo to distinguish the hand of man.

Claims 77-82 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to a 'reconstituted animal embryo' and an 'animal'. As written, the claims read on cells that are a human embryo and a human being. A human being or human embryo is not-statutory subject matter. See 1077 O.G. 24, April 21, 1987. Amending the claims to encompass 'a non-human animal' would obviate the basis of the rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-50 and 56-88 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims1-16 of U.S. Patent No. 6,525,243 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '243 are open to include more method steps than specifically recited to accomplish reconstituting the embryo. In particular, the specification provides several methods to increase the yields of viable embryos, including the use of serial nuclear transfer (column 7, lines 55-67). It would be obvious to increase the yield or to optimize the specifically claimed invention by using the additional method steps provided in the teachings of the disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 77, 80-82 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US Patent 5,843,780 A).

Claim 77 is drawn to a reconstitute embryo and claims 80-83 encompass cell populations obtained from an embryo made by the method of claim 42. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 42-50 and 56-88 are rejected under 35 U.S.C. 102(e) as being anticipated by Stockman Campbell *et al.* (US Patent 6,525,243 B1).

Stockman Campbell *et al.* teach a method of nuclear transfer comprising the transfer of a somatic cell into a recipient oocyte. Stockman Campbell *et al.* provide detailed guidance for the timing of the insertion of the nuclear material into the oocyte, activation and general methodology to culture the resulting nuclear transfer unit into a viable embryo and ultimately cloned animal (see claim 1). In addition, Stockman Campbell *et al.* teach that the methodology can be improved to provide increased yields through the use of serial nuclear transfer (starting at the bottom of column 7). Stockman Campbell *et al.* teach that the method can be used for any animal anticipating the specific species set forth in dependent claims. Thus, Stockman Campbell *et al.* provide each of the specific method steps set forth in the claims.

Claims 42-50 and 56-88 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

In this case the '243 lists two inventors for the claimed method that includes at least round of nuclear transfer. The claim language of the allowed claims is open allowing for additional method steps to be performed. The specification of '243 provides reasons and guidance for additional method steps, including the serial transplantation using nuclear transfer technology as instantly claimed. However, the instant application only provides one inventor even though the claimed method of '243 would have to be practiced in practicing the instantly claimed method. It is unclear why the second inventor listed on '243, Ian Wilmut, is not listed as an inventor on the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42-50 and 56-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell *et al.* (WO 97/07669), Gurdon (J Cell Sci 4 :287-318, 1986) and Stice *et al.* (Biol of Reprod, 48 :715-719,1993).

At the time of filing, the methodology of nuclear transfer was a subject of active research and reviewing the state of the art Gurdon teaches that as early as 1986, transferring donor nuclear into enucleated oocytes was accomplished in a variety of species from amphibians to mammals. Gurdon summarizes several lines of experiments of the reprogramming affect of the oocyte, indicating that it is factors in the cytoplasm not the nucleus that are important in reprogramming and that the reprogramming is exerted rapidly (bottom of page 309). Success in mammals was accomplished as early as 1981, however it was noted that not all stages of cells could be reprogrammed, and that in the mouse successful nuclear transplantation and blastula formation using a mouse embryo was limited to a one/two cell stage. Prather *et al.* provide a similar summary at a later date, noting similarities and differences among amphibians and mammals tested. Interestingly, it was noted that late reprogramming is thought to vary depending upon the degree of differentiation, and the more differentiated the cell was the more difficult it may be to reprogram the donor cell (page 232). More specifically regarding the mouse, it was noted that

there was a major shift in control at the two cell stage and reprogramming past this stage could require major reprogramming (page 232). Campbell *et al.* provide more detailed guidance for the methodology and techniques required to successfully use nuclear transfer with quiescent cells in mammals. Similar to the teachings of Gurdon and Prather *et al.*, Campbell *et al.* teach that quiescent cells like cells from later stage embryos have cells that are more differentiated and may require more reprogramming. One strategy for increasing the efficiency it through the use of serial nuclear transplantation (page 16). All teach that the cytoplasm of an oocyte contains the factors capable of reprogramming a donor nuclei, and that as an embryo grows and the first cell divides the capability of any single embryonic cell to be capable of giving rise to a cloned animal decreases with each division. This differentiation can occur as early as the first division as demonstrated for the mouse. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to increase the efficiency of reprogramming of a donor nuclei serial nuclear transplantation could be used as suggested by Campbell *et al.* It was known that reprogramming is affected by the oocyte cytoplasm and the resulting dividing nuclear transfer embryo represents a differentiated cell type with each cell division, therefore, to affect the greatest amount of reprogramming during serial nuclear transplantation one having ordinary skill in the art would have been motivated to perform nuclear transfer methodology at the earliest stage of embryo development. This would be generally applicable for use in all animals and particular important in mammals such as the mouse where differentiation occurs as early as the first division. The techniques of nuclear transfer were well known at the time of filing as well as the physiological similarities and differences among the animal cells used in such techniques, and there would have been a reasonable expectation of

success given the successful summarized in each of the references. Moreover, there would have been a reasonable expectation that the serial transplantation of a donor nuclei could be used to more fully re-program the nuclei, in particular for use with donor cells from different species such as the mouse or with a donor cell source representing cells that were more difficult to re-program with only one round of nuclear transfer.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

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